

Synthesis of H-TAP-Boc molecule

Synthesis of Cbz-TAP



FIG. 1A

Synthesis of Cbz-TAP-Boc

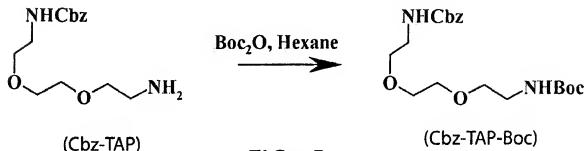


FIG. 1B

Synthesis of Boc-TAP

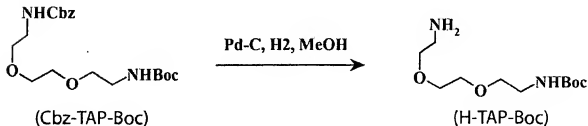


FIG. 1C

## Attaching Spacer to Peptide with C-Terminus

Peptide with free C-terminus:

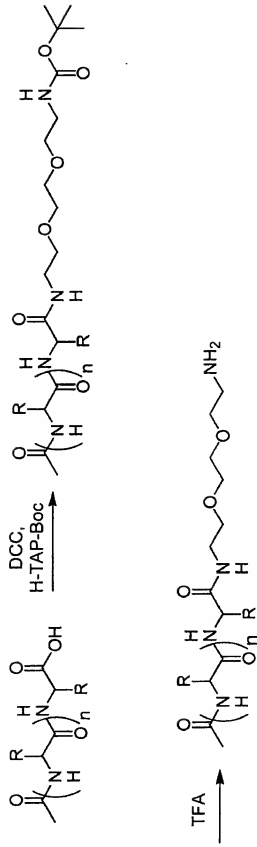


FIG. 2

## Attaching Spacer to Peptide with Free Side-Chain Acid

Peptide with free side-chain acid:

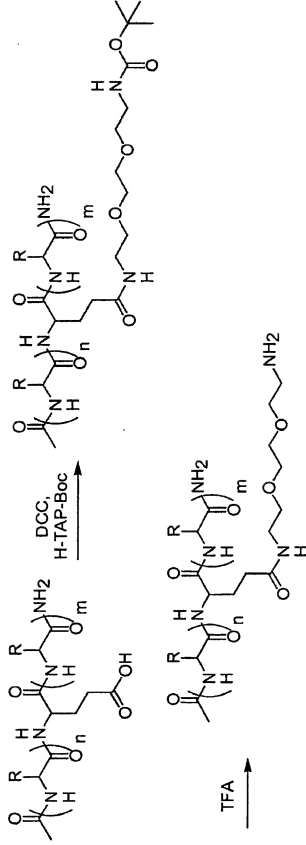


FIG. 3

# PEGylation of Peptide, with mPEG-NPC

Peptide with TAP on C-terminus:

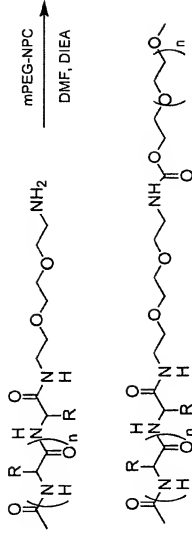


FIG. 4A

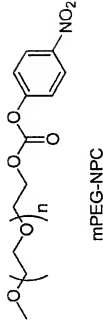


FIG. 4B

## PEGylation of Peptide, with mPEG-SPA

Peptide with TAP on C-terminus:

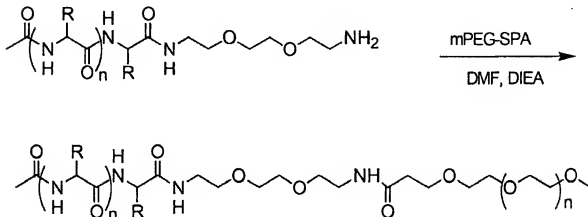
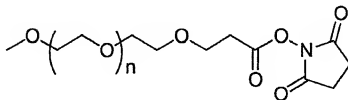


FIG. 5A



mPEG-SPA

FIG. 5B

# Attaching Spacer and Synthesizing Peptide

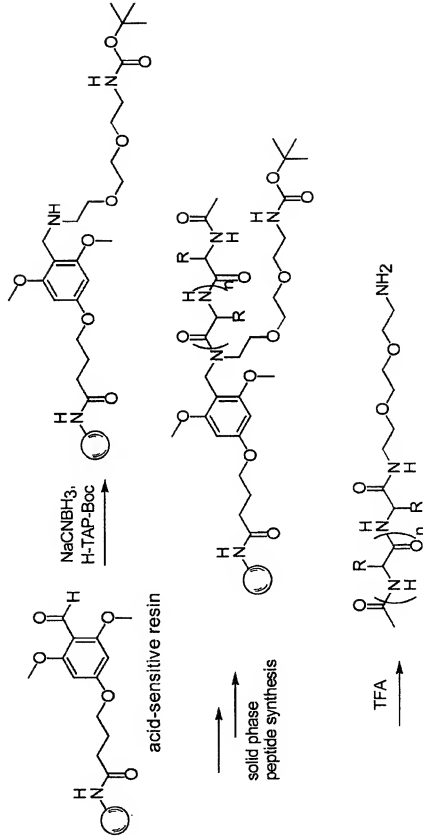


FIG. 6

# Synthesis of Peptide Dimer with Spacer, Attached to Resin Synthesis of TentaGel-Linker:

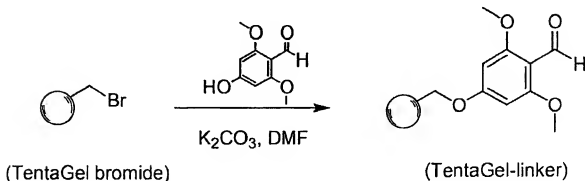


FIG. 7A

## Synthesis of TentaGel-Linker-TAP(Boc)

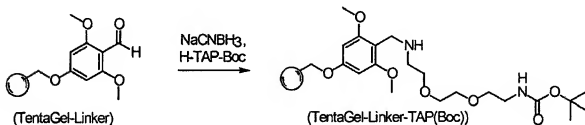


FIG. 7B

## Synthesis of TentaGel-Linker-TAP-Lys

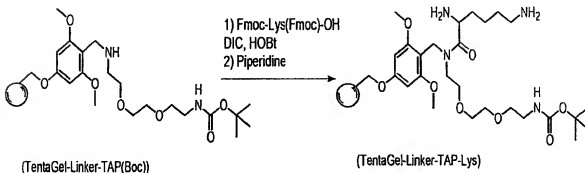


FIG. 7C





# Cleavage from Resin

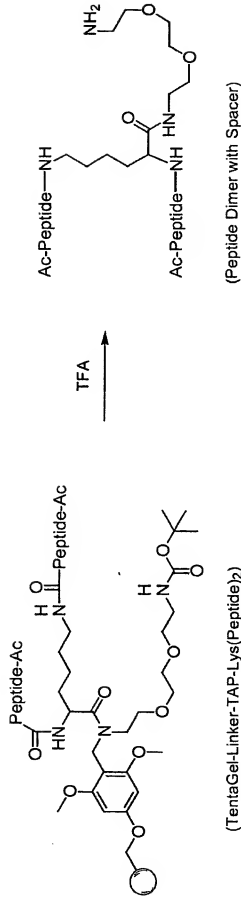


FIG. 7E

## Oxidation

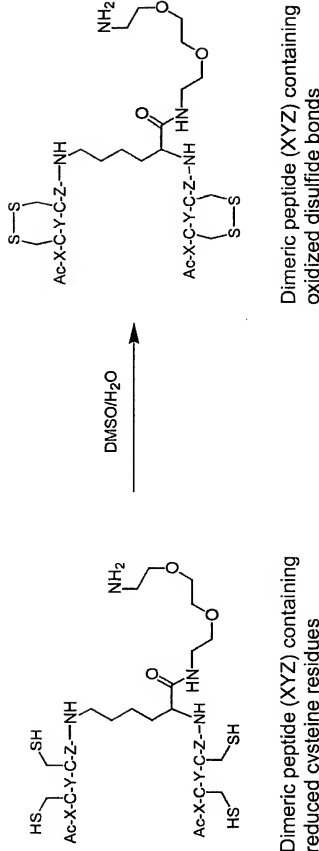


FIG. 7F

### PEGylation of Peptide Dimer with Spacer, with mPEG-NPC

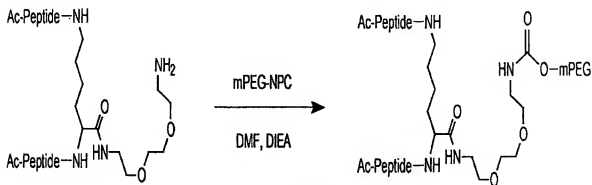


FIG. 8A

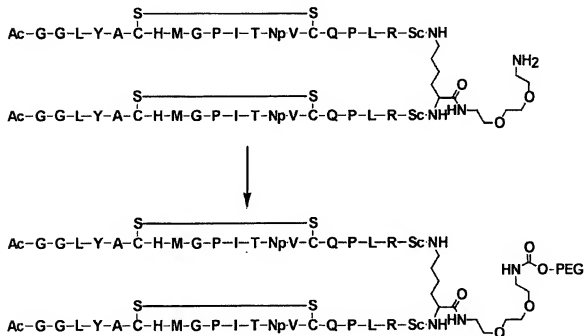
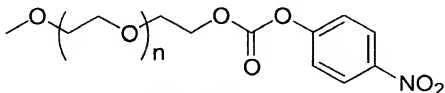


FIG. 8B



mPEG-NPC  
FIG. 8C

# PEGylation of Peptide Dimer with Spacer, with mPEG-SPA

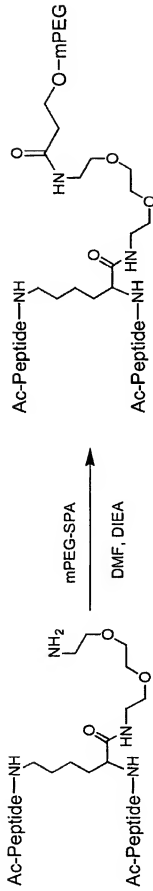


FIG. 9A

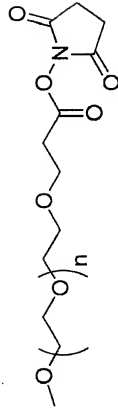


FIG. 9B

## Ion Exchange Purification

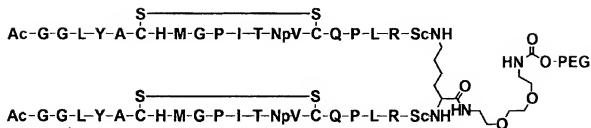
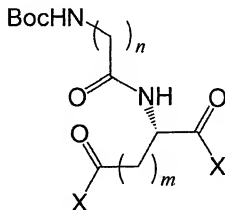


FIG. 10



$m=1-5$ ,  $n = 1-14$ ,  $m$  and  $n$  are integers

FIG. 11A

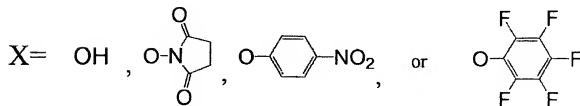
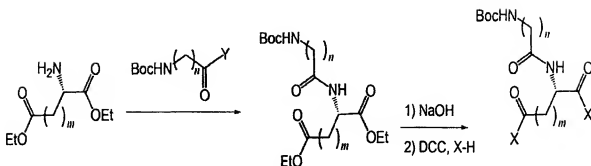
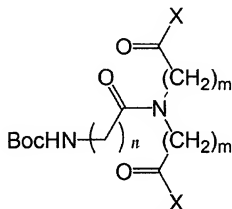


FIG. 11B



$m=1-5$ ,  $n = 1-14$ ,  $m$  and  $n$  are integers

FIG. 11C



$m=1-5$ ,  $n = 1-14$ ,  $m$  and  $n$  are integers

FIG. 12A

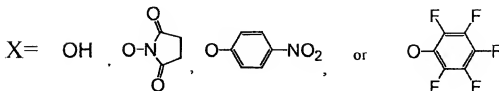
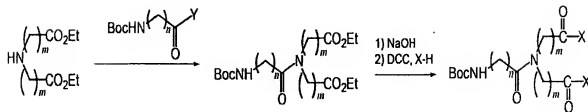


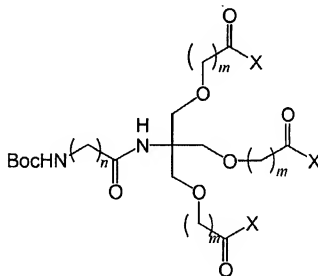
FIG. 12B



$m=1-5$ ,  $n=1-14$ ,  $m$  and  $n$  are integers

FIG. 12C

Synthesis of Homotrifunctional Molecules  
 Branched homotrifunctional molecules having the structure



$m=1-2$ ,  $n=1-6$ ,  $m$  and  $n$  are integers

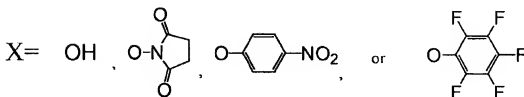
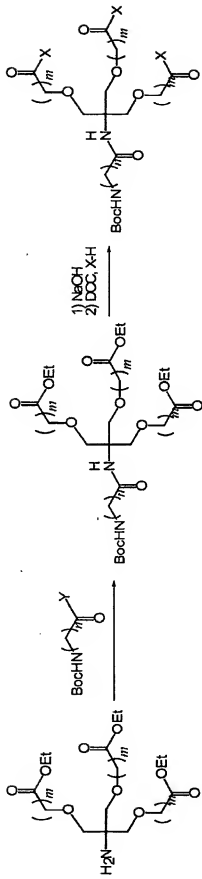


FIG. 13A



$m=1-2$ ,  $n = 1-6$ ,  $m$  and  $n$  are integers

FIG. 13B



C-Terminus Dimerization and PEGylation Using A Trifunctional Molecule  
A trifunctional molecule having the structure

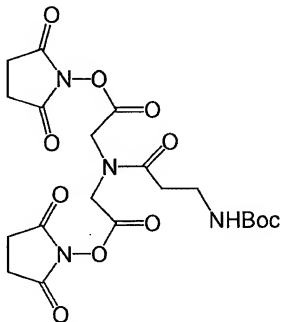


FIG. 14A

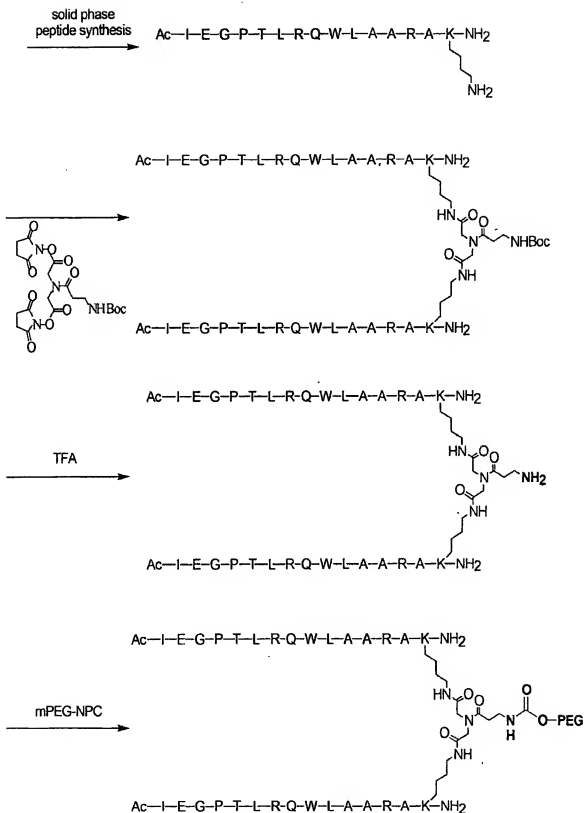


FIG. 14B

# N-Terminus Dimerization and PEGylation Using A Trifunctional Molecule

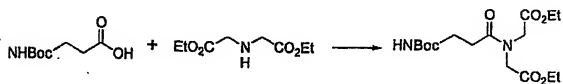


FIG. 15A

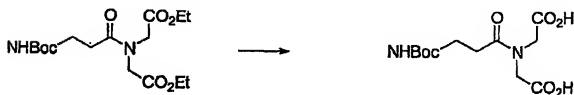


FIG. 15B

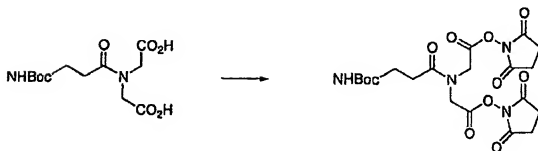


FIG. 15C

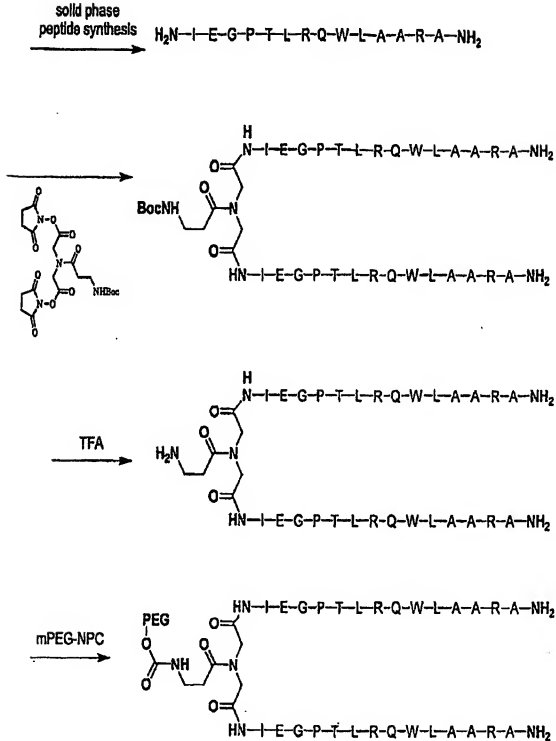


FIG. 15D

A trifunctional molecule having the structure

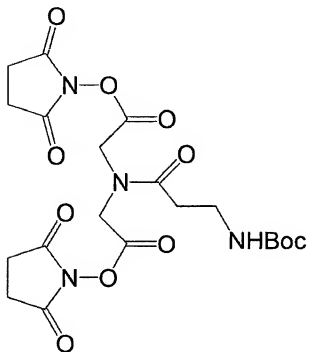


FIG. 16A

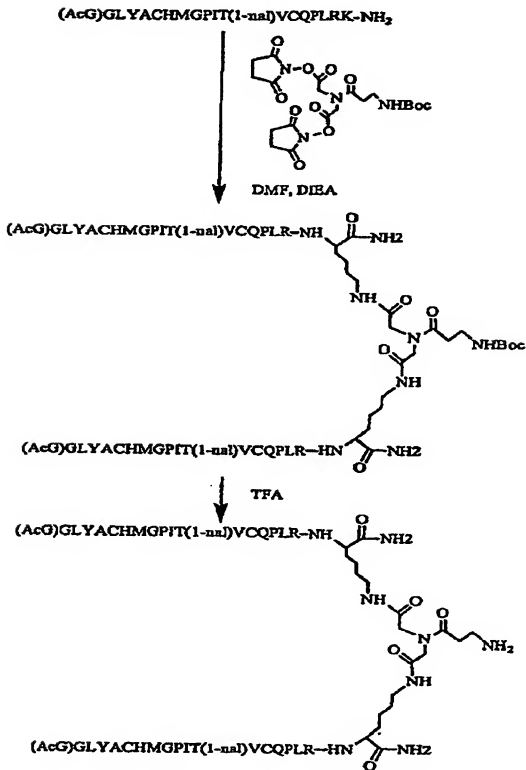


FIG.16B

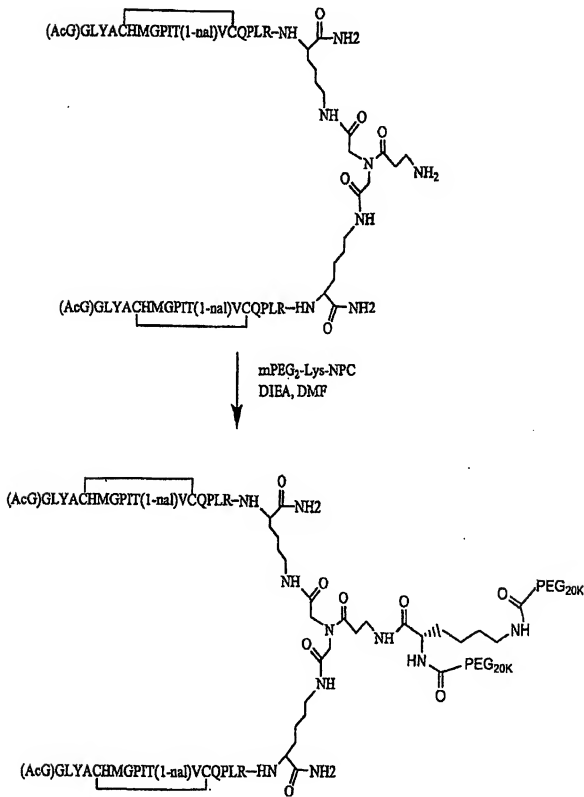


FIG. 16C

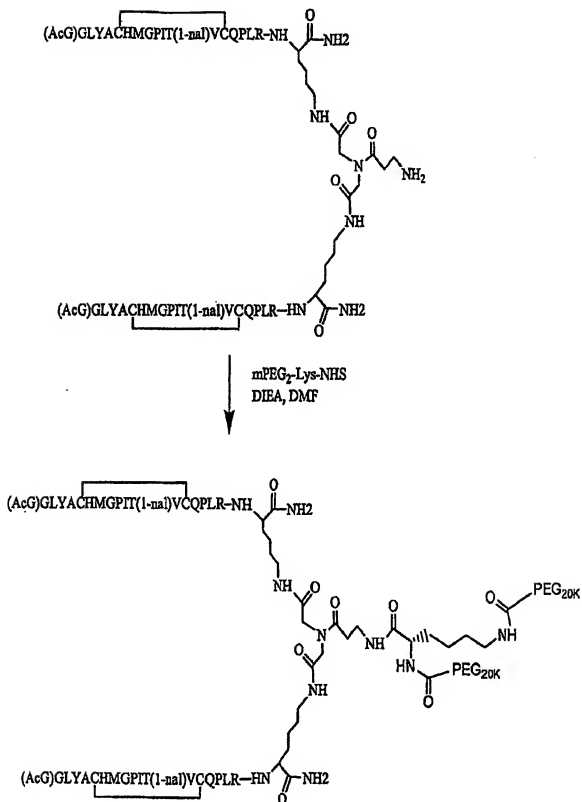


FIG. 16D